In vitro study of the long-term cortisol treatment effects on the growth rate and proliferation of the neural stem/precursor cells

Alireza Abdanipour[1], Mohsen Sagha[2], Ali Noori-Zadeh[1], Iraj Pakzad[3], Taki Tiraihi[1]

[1]Shefa Neuroscience Research Center, Khatam Al-Anbia Hospital, Tehran, Iran, [2]Department of Anatomical Sciences and Pathology, Research Laboratory for Embryology and Stem Cells, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran, [3]Department of Microbiology, Faculty of Medicine, Ilam University of Medical Sciences, Ilam, Iran

Adult neural stem/precursor cells (NSPCs) residing in the subventricular zone of the lateral ventricles and the subgranular zone of the dentate gyrus of the hippocampus are involved in the memory formations and psychological problems. It is believed that basal levels of glucocorticoids are essential for neuronal development, plasticity, and survival, while stress-mediated levels of glucocorticoids produce neuronal loss. Degeneration of NSPCs by the apoptotic and necrotic stimuli have great devastating outcomes on the brain and contributes to the pathophysiology of neurological as well as psychological disorders. Using MTT assay, acridine orange, and TUNEL assay, we have demonstrated that cortisol at high and excessive (more than 5 μM) levels had anti-proliferative effects on the NSPCs derived from subventricular and subgranular zones in a dose- and time-dependent manner through apoptosis as well as necrosis. These outcomes can highlight the role of stress-mediated decline of adult neurogenesis in the aging brain and interconnect stress-mediated cortisol secretion with brain aging diseases.

Keywords: Cortisol, NSPCs, Adult neurogenesis, Subventricular zone, Dentate gyrus, Neurosphere

Introduction

Adult neurogenesis or the production of new neural stem/precursor cells (NSPCs) has been shown to occur in two major regions of the brain including the subventricular zone of the lateral ventricles and the subgranular zone of the dentate gyrus of the hippocampus. In the dentate gyrus, thousands of granule cells were born daily; however, only a small portion of the NSPCs survives and develops into mature granule cells.[1] It has been shown that adult neurogenesis is the key component of the pattern separation function of the dentate gyrus, and recent studies also shed light on the significant relationships between adult neurogenesis and cognition.[2–4] The functional theories of new NSPCs production have consolidated several aspects of adult neurogenesis and maturation.[5] The immature granule cells demonstrate an increased intrinsic excitability and plasticity,[6,7] and interestingly, it is believed that this immature state of granule cells represents a critical developmental period in which they encode significant features of their environments.[8,9] Dentate gyrus and cornu ammonis 3 interact via the mossy fibers to process high-resolution spatial information.[10–12] Further, the dentate gyrus has been proposed to mediate spatial pattern separation of similar spaces for the detection of small changes within an environment. It is presumed that cornu ammonis 3 mediates a similar pattern separation process on much larger scale spaces,[11] and they may contribute to neurological problems such as Alzheimer's disease (AD). Moreover, NSPCs located within the subventricular zone exert an innate homeostatic regulatory function protecting striatal neurons from glutamate-mediated excitotoxicity[13], and thus adult neurogenesis may potentially play a crucial role in Huntington's disease (HD) as well, in which loss of the striatal projection neurons occurs.[14] Moreover, striatum is the main input nucleus of the basal ganglia and a key neural substrate for procedural learning and memory.[15] The vast majority of the striatal neurons are GABAergic

Correspondence to: Alireza Abdanipour, Shefa Neuroscience Research Center, Khatam Al-Anbia Hospital, Tehran, Iran. Email: abdani.anatomy@yahoo.com

DOI 10.1179/1743132814Y.0000000431